

***What Is Claimed Is:***

1. An isolated polynucleotide encoding a first antibody at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising an amino acid sequence selected from the group consisting of:

- (a) at least one CDR region of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- (b) at least two CDR regions of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- (c) at least three CDR regions of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- (d) at least one CDR region of a VL domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- (e) at least two CDR regions of a VL domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8,

XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5,  
XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and  
XF27/28.43E2; and

- (f) at least three CDR regions of a VL domain of the antibody  
expressed by a hybridoma cell line selected from the group  
consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8,  
XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5,  
XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and  
XF27/28.43E2.

2. The isolated polynucleotide of claim 1, wherein said first antibody is at  
least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least  
100% identical to a second antibody comprising the VH domain of the  
antibody expressed by the hybridoma cell line selected from the group  
consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

3. The isolated polynucleotide of claim 1, wherein said first antibody is at  
least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least  
100% identical to a second antibody comprising the VL domain of the

antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

4. The isolated polynucleotide of claim 1, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

5. The isolated polynucleotide of claim 1, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VL domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

6. The isolated polynucleotide of claim 1, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the VL domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;

- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

7. The isolated polynucleotide of claim 1, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the constant domain and the VL domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

8. The isolated polynucleotide of claim 4, wherein said constant domain is selected from the group consisting of an IgG constant domain, an IgA constant domain, and a IgM constant domain.

9. The isolated polynucleotide of claim 5, wherein said constant domain is a kappa constant domain or a lambda constant domain.

10. The isolated polynucleotide of claim 1, wherein said first antibody is a Fab fragment, an Fab' fragment, an F(ab')<sub>2</sub>, an Fv, a single chain Fv, or a disulfide linked Fv.

11. The isolated polynucleotide of any one of claims 1 to 10, wherein said first antibody is a monoclonal antibody.

5 12. The isolated polynucleotide of any one of claims 1 to 10, wherein said first antibody immunospecifically binds to an extracellular portion of G-protein Chemokine Receptor (CCR5) polypeptide selected from the group consisting of:

- 10 (a) N-terminal extracellular region;  
(b) extracellular loop 1;  
(c) extracellular loop 2; and  
(d) extracellular loop 3.

13. The isolated polynucleotide of any one of claims 1 to 10, wherein said first antibody is a human antibody.

14. The isolated polynucleotide of any one of claims 1 to 10, wherein said first antibody is a humanized antibody.

15 15. The isolated polynucleotide of any one of claims 1 to 10, wherein said polynucleotide is fused to a heterologous polynucleotide.

16. A vector comprising the isolated polynucleotide of any one of claims 1 to 10.

25 17. A host cell comprising the vector of claim 16.

18. A host cell comprising the isolated polynucleotide of any one of claims 1 to 10.

19. A method of making an antibody comprising:

- 30 (a) expressing the antibody encoded by the isolated polynucleotide of any one of claims 1 to 10; and  
(b) recovering said antibody.

20. The antibody made by the method of claim 19.
21. An isolated first antibody at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising an amino acid sequence selected from the group consisting of:
- 5
- (a) at least one CDR region of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- 10
- (b) at least two CDR regions of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- 15
- (c) at least three CDR regions of a VH domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- 20
- (d) at least one CDR region of a VL domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2;
- 25
- (e) at least two CDR regions of a VL domain of the antibody expressed by a hybridoma cell line selected from the group
- 30

consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and XF27/28.43E2; and

- 5 (f) at least three CDR regions of a VL domain of the antibody expressed by a hybridoma cell line selected from the group consisting of: XF3.5F1, XF11.1F8, XF3.6A2, XF3.10B8, XF22.3C9.6, XF22.9E6, XF27/28.7D5, XF27/28.18B5, XF27/28.25G10, XF27/28.36A12, XF27/28.36F11, and
- 10 XF27/28.43E2.

22. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- 15 (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- 20 (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- 25 (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

30 23. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VL domain of the



antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

24. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

25. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VL domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

26. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the VL domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;

- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

5

27. The isolated first antibody of claim 21, wherein said first antibody is at least 95%, at least 96%, at least 97%, at least 98%, at least 99%, or at least 100% identical to a second antibody comprising the VH domain and the constant domain and the VL domain and the constant domain of the antibody expressed by the hybridoma cell line selected from the group consisting of:

10

- (a) XF3.5F1;
- (b) XF11.1F8;
- (c) XF3.6A2;
- (d) XF3.10B8;
- (e) XF22.3C9.6;
- (f) XF22.9E6;
- (g) XF27/28.7D5;
- (h) XF27/28.18B5;
- (i) XF27/28.25G10;
- (j) XF27/28.36A12;
- (k) XF27/28.36F11; and
- (l) XF27/28.43E2.

15

20

28. The isolated polynucleotide of claim 24, wherein said constant domain is selected from the group consisting of an IgG constant domain, an IgA constant domain, and a IgM constant region.

25

29. The isolated polynucleotide of claim 25, wherein said constant domain is a kappa constant domain or a lambda constant domain.

30

30. The isolated first antibody of claim 21, wherein the isolated first antibody is a Fab fragment, an Fab' fragment, an F(ab')<sub>2</sub>, an Fv, a single chain Fv or a disulfide linked Fv.

31. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody immunospecifically binds to G-protein Chemokine Receptor (CCR5) polypeptide.

32. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody immunospecifically binds to an extracellular portion of G-protein Chemokine Receptor (CCR5) polypeptide selected from the group consisting of:

- (a) N-terminal extracellular region;
- (b) extracellular loop 1;
- (c) extracellular loop 2; and
- (d) extracellular loop 3.

33. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody is a monoclonal antibody, a human antibody, or a humanized antibody.

34. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody has a dissociation constant ( $K_D$ ) selected from the group consisting of:

- (a) a dissociation constant ( $K_D$ ) of at least  $10^{-7}$  M;
- (b) a dissociation constant ( $K_D$ ) of at least  $10^{-8}$  M;
- (c) a dissociation constant ( $K_D$ ) of at least  $10^{-9}$  M;
- (d) a dissociation constant ( $K_D$ ) of at least  $10^{-10}$  M;
- (e) a dissociation constant ( $K_D$ ) of at least  $10^{-11}$  M; and
- (f) a dissociation constant ( $K_D$ ) of at least  $10^{-12}$  M.

35. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody has an off-rate selected from the group consisting of:

- (a) an off-rate of at least  $10^{-3}$ /sec;
- (b) an off-rate of at least  $10^{-4}$ /sec;

- (c) an off-rate of at least  $10^{-5}$ /sec;
- (d) an off-rate of at least  $10^{-6}$ /sec; and
- (e) an off-rate of at least  $10^{-7}$ /sec.

5 36. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody is an agonist of a G-protein Chemokine Receptor (CCR5).

10 37. The isolated first antibody of any one of claims 21 to 30, wherein the isolated first antibody is an antagonist of a G-protein Chemokine Receptor (CCR5).

15 38. The isolated first antibody of any one of claims 21 to 30, wherein said antibody has an activity selected from the group consisting of:

- (a) neutralization of G-protein Chemokine Receptor (CCR5);
- (b) inhibition of Eotaxin binding to G-protein Chemokine Receptor (CCR5) expressing cells;
- (c) inhibition of Eotaxin induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;
- (d) inhibition of RANTES binding to G-protein Chemokine Receptor (CCR5) expressing cells;
- (e) inhibition of RANTES induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;
- (f) inhibition of MCP-1 binding to G-protein Chemokine Receptor (CCR5) expressing cells;
- (g) inhibition of MCP-1 induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;
- (h) inhibition of MCP-2 binding to G-protein Chemokine Receptor (CCR5) expressing cells;
- (i) inhibition of MCP-2 induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;

(j) inhibition of MCP-3 binding to G-protein Chemokine Receptor (CCR5) expressing cells;

(k) inhibition of MCP-3 induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;

5 (l) inhibition of MIP-1alpha binding to G-protein Chemokine Receptor (CCR5) expressing cells;

(m) inhibition of MIP-1alpha induced chemotaxis to G-protein Chemokine Receptor (CCR5) expressing cells;

10 (n) inhibition of MIP-1beta binding to a G-protein Chemokine Receptor (CCR5);

(o) inhibition of MIP-1beta induced chemotaxis of G-protein Chemokine Receptor (CCR5) expressing cells;

(p) downregulation of G-protein Chemokine Receptor (CCR5) expression; and

15 (q) upregulation of G-protein Chemokine Receptor (CCR5) expression.

20 39. The isolated first antibody of any one of claims 21 to 30, wherein said antibody has an activity selected from the group consisting of:

(a) inhibition of HIV viruses to bind to G-protein Chemokine Receptor (CCR5) expressing cells; and

(b) inhibition of HIV viruses to infect G-protein Chemokine Receptor (CCR5) expressing cells.

25 40. The isolated first antibody of claim 21, wherein the isolated first antibody is coupled or conjugated to a detectable label or to a radioactive label.

30 41. The isolated first antibody of claim 40, wherein the detectable label is an enzyme, a fluorescent label, a luminescent label, or a bioluminescent label.

42. The isolated first antibody of claim 21, wherein the isolated first antibody is coupled or conjugated to a heterologous polypeptide.

43. The isolated first antibody of claim 21, wherein the isolated first antibody is conjugated to a therapeutic agent.

44. The isolated first antibody of claim 43, wherein the therapeutic agent is an antimetabolite, an alkylating agent, an antibiotic, a growth factor, a cytokine, or an anti-angiogenic agent.

45. The isolated first antibody of claim 43, wherein the therapeutic agent is an anti-mitotic agent, an anthracycline, a toxin, or an apoptotic agent.

46. The isolated first antibody of claim 21, wherein the isolated first antibody is conjugated to a cytotoxic agent.

47. An antibody that binds the same epitope on a G-protein Chemokine Receptor (CCR5) polypeptide as the isolated first antibody of any one of claims 21 to 30.

48. The isolated first antibody of any one of claims 21 to 30, in a pharmaceutically acceptable carrier.

49. A cell line engineered to express the isolated first antibody of any one of claims 21 to 30.

50. The isolated first antibody expressed from the cell line of claim 49.

51. A method of treating, preventing or ameliorating a disease or disorder comprising administering the isolated first antibody of any one of claims 21 to 30, or 40 to 46, to an animal.

52. The method of claim 51, wherein the animal is a human.

53. The method of claim 51, wherein the disease or disorder is selected from the group consisting of:

- (a) a disease or disorder associated with inflammation;
- (b) a disease or disorder associated with defective or aberrant chemotaxis of immune cells;
- (c) a disease or disorder associated with defective or aberrant T-cell antigen presenting cell interaction;
- (d) an infectious disease;
- (e) an autoimmune disease;
- (f) Rheumatoid Arthritis;
- (g) a neurodegenerative disorder;
- (h) a viral infection;
- (i) HIV infection;
- (j) an early stage HIV infection;
- (k) a cytomegalovirus infection;
- (l) a poxvirus infection;
- (m) a *Pneumocystis carinii* infection;
- (n) Kaposi's sarcoma;
- (o) a disease or disorder associated with aberrant G-protein Chemokine Receptor (CCR5) expression;
- (p) a disease or disorder associated with the lack of G-protein Chemokine Receptor (CCR5) function;
- (q) a disease or disorder associated with aberrant G-protein Chemokine Receptor (CCR5) ligand expression; and
- (r) a disease or disorder associated with the lack of G-protein Chemokine Receptor (CCR5) ligand function.

54. The method of claim 51, wherein the isolated first antibody is administered in combination with a chemotherapeutic agent.



55. The method of claim 51, wherein the isolated first antibody is administered in combination with anti-retroviral therapy.

56. The method of claim 51, wherein the isolated first antibody is administered prophylactically to the animal.

57. A method of detecting expression of a G-protein Chemokine Receptor (CCR5) polypeptide comprising:

(a) assaying the expression of a G-protein Chemokine Receptor (CCR5) polypeptide in a biological sample from an individual using the isolated first antibody of claim 21; and

(b) comparing the level of a G-protein Chemokine Receptor (CCR5) polypeptide with a standard level of a G-protein Chemokine Receptor (CCR5) polypeptide, (*e.g.*, the level in normal biological samples).

58. A method of detecting, diagnosing, prognosing, or monitoring cancers and other hyperproliferative disorders comprising:

(a) assaying the expression of a G-protein Chemokine Receptor (CCR5) polypeptide in a biological sample from an individual using the isolated first antibody of claim 21; and

(b) comparing the level of a G-protein Chemokine Receptor (CCR5) polypeptide with a standard level of a G-protein Chemokine Receptor (CCR5) polypeptide.

59. A kit comprising the isolated first antibody of claim 21.

60. The kit of claim 59 comprising a control antibody.